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PATENT
Attorney Docket No. 3495.0004-04

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of:	)	
	)	
Luc MONTAGNIER et al.	)	Group Art Unit: 1813
	)	
Serial No.: 08/067,148	)	Examiner: J. Parkin
	)	
Filed: May 26, 1993	)	

For: ANTIBODIES WHICH BIND WITH PROTEINS OF HUMAN IMMUNODEFICIENCY VIRUS TYPE 1 (HIV-1), AND IMMUNE COMPLEXES COMPRISING PROTEINS OF HIV-1 (As Amended)

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

APPEAL BRIEF PURSUANT TO 37 C.F.R. § 1.192(a)

Pursuant to 37 C.F.R. § 1.192, appellants submit this Appeal Brief, in triplicate, along with the requisite fee pursuant to 37 C.F.R. § 1.17(f), to the Board of Patent Appeals and Interferences from the Final Rejection dated May 29, 1996 (Paper No. 27). Appellants filed a Notice of Appeal on November 29, 1996, from the final rejection of claims 29-31.

I. REAL PARTY IN INTEREST

The real party in interest in the pending appeal is the assignee, Institut Pasteur of Paris, France, by virtue of an assignment by appellants, duly recorded.

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II. RELATED APPEALS AND INTERFERENCES

There are no other appeals or interferences known to the appellants, the undersigned, or the assignee that will directly affect or be directly affected by or have a bearing on the Board's decision in this Appeal.

III. STATUS OF CLAIMS

Claims 15, 16, 18-20, and 29-31 are pending in this application. Claims 1-14, 17, and 21-28 have been canceled. Claims 15, 16, and 18-20 are allowed.

The pending claims are set forth in Exhibit 1. Claims 29-31 are the claims on appeal.

IV. STATUS OF AMENDMENTS

All amendments submitted by the appellants have been entered.

V. SUMMARY OF INVENTION

The invention relates to the discovery and isolation of lymphadenopathy retroviruses (LAV), also known as human immunodeficiency viruses (HIV), which have been detected in AIDS patients. Appellants purified several molecules from HIV-1 and identified them as proteins. Some of the proteins isolated from HIV-1, such as p12 and p18, have been found to provide discriminating identification of HIV-1 infection in patients, because these proteins are

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only found in HIV-1 retroviruses. Thus, these proteins are useful for detecting the presence or absence of HIV-1, particularly by means of immunoassays.

Antibodies against the p12 and p18 proteins are also of interest. When a foreign substance or antigen is introduced into the body, the immune system elicits the production of antibodies that specifically bind with the antigen to form an antigen-antibody or immunological complex, which is then targeted for destruction and removal from the body. For example, when an antigen, such as p12 or p18, is introduced into the body, antibodies that specifically bind to the p12 or p18 antigen are produced. The detection of antibodies that bind to p12 or p18 in a biological sample is correlated with the presence of HIV-1.

The invention of the claims at issue involves immunological complexes of p12 or p18 of HIV-1. Specifically, independent claims 29-30 are directed to immunological complexes comprising purified p12 or p18 protein of HIV-1 and an antibody that binds with the protein.

Dependent claim 31 specifies that the protein of the immunological complex is labeled with an immunoassay label selected from the group consisting of a radioactive label, an enzymatic label, a fluorescent label, a chemiluminescent label, and a chromophore label.

The immunological complexes can be produced in the body or outside the body. For example, in an immunoassay to detect the presence of a labeled antibody against p12 or p18 in a biological sample, the p12 or p18 antigen can be placed on a solid support, and the biological sample containing antibodies can be contacted with the support. After washing, the antigen-antibody (immune) complex can be detected by screening for the labeled antibody bound to the

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p12 or p18 antigen on the solid support. Detection of an immunological complex in this fashion is indicative of the presence of antibodies against p12 or p18 in the biological sample and, accordingly, an indication of HIV infection.

Alternatively, the immunoassay may be used to detect the presence of p12 or p18 antigen in a biological sample. In this case, the antibody can be bound to a solid support. Labeled p12 or p18 antigen contained in the biological sample will bind to the antibody on the solid support. Detection of the antigen-antibody (immune) complex is indicative of the presence of the p12 or p18 antigen and HIV infection.

It is evident that immunological complexes are useful. They are, in fact, the end point for the detection of HIV infection in biological samples using immunoassay techniques.

VI. ISSUE

Whether the invention of claims 29-31 directed to immunological complexes of p12 or p18 and an antibody that binds to p12 or p18, respectively, is supported and adequately described by appellants' specification under 35 U.S.C. § 112, first paragraph.

VII. GROUPING OF CLAIMS

Pursuant to 37 C.F.R. § 1.192(c)(7), independent claim 29 and dependent claims 30-31 stand or fall together, as argued.

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VIII. ARGUMENT

In the Office Action mailed May 29, 1996 (Paper No. 27), claims 29-31 were finally rejected under 35 U.S.C. § 112, first paragraph, as the specification allegedly does not provide support for the invention as claimed. In particular, the Examiner asserted that the term "immunological complex" as recited in claims 29-31 is not supported. The rejection concedes that "immunocomplexes" and "immune complexes" are explicitly recited in the specification. (Paper No. 27 at 1). Nevertheless, the Examiner stated that

> . . . this brief recitation is not sufficient to provide support for the instantly claimed immunological complexes involving the viral antigens p12 or p18 and antibodies directed against said antigens. The specification does not disclose the contemplation, preparation, purification, or associated use of these immune complexes.

(Paper No. 27 at 1-2). Accordingly, the rejection is based upon a lack of written description.

Appellants respectfully traverse the rejection.

The function of the written description requirement under the first paragraph of 35 U.S.C. § 112 is to clearly convey the subject matter that an applicant has invented as of the filing date of the application relied on. In re Barker, 559 F.2d 588, 592 n.4, 194 U.S.P.Q. 470, 473 n.4 (C.C.P.A. 1977), cert. denied, 434 U.S. 1064 (1978). The applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he was in possession of the invention, i.e., whatever is now claimed. Vas-Cath Inc. v. Mahurkar, 19 U.S.P.Q.2d 1111, 1117 (Fed. Cir. 1991).

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A. The Specification Literally Supports The Immune Complexes Of The Claimed Invention

Appellants' specification literally supports the immune complexes of the claimed invention, for example, at page 12, lines 14-15, where it is stated that "[i]mmunocomplexes were analyzed by polyacrylamide gel electrophoresis under denaturing conditions." At page 15, lines 9-12, appellants describe "diagnostic compositions containing one or more of the proteins which immunologically react with the antibodies in the biological fluid of the patient," and appellants specifically teach that these compositions "are useful for determination of the infection or its absence." The description elaborates that these diagnostic compositions preferably comprise the p12 or p18 protein. (Specification at page 15, lines 4-9). In addition, page 21, lines 8-9 and the legend of Figure 5 on page 37 of the original specification specify that immunocomplexes were isolated by immobilization on Sepharose beads, a common method of purifying antibodies and immune complexes.

In fact, appellants' contemplation of the claimed immunological complexes is supported by original claim 1, which is reproduced for the convenience of the Board:

> 1. An in vitro diagnostic method for detecting the presence or absence of antibodies to proteins of the lymphadenopathy retrovirus (LAV), the etiological agent of LAS or AIDS, which method comprises:
>
> contacting a biological sample capable of containing LAV antibodies of a patient to be diagnosed for the presence or absence of such antibodies with a composition containing a p18 protein of a lysate of the lymphadenopathy retrovirus (LAV);

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> detecting **the immunological formation of a complex** of LAV antibodies in the biological sample and of the composition containing the LAV p18 protein as a positive diagnosis that the patient does have LAV antibodies or the absence of the complex as a diagnosis that the patient does not have the LAV antibodies, the lymphadenopathy virus being immunologically distinct from the T leukemia viruses HTLV, including the virus HTLV I.

(Emphasis added). See also original claims 7, 9, and 14. As stated above, "LAV" is another name for HIV.

While literal support for claim language is not the appropriate standard for 35 U.S.C. § 112, first paragraph, (see, Vas-Cath Inc. v. Mahurkar, 19 U.S.P.Q.2d at 1563, 19 U.S.P.Q.2d at 1117), appellants submit that the terms used in their specification are as close to the literal support for "immunological complexes" recited in claims 29-31 as one skilled in the art would need to conclude that appellants were in possession of the invention as now claimed.

B. The Specification Clearly Demonstrates That Appellants Contemplated And Possessed The Claimed Immunological Complexes

Under the written description requirement of the first paragraph of § 112, appellants need only show that they were in possession of the claimed invention. Vas-Cath Inc. at 1563-1564, 19 U.S.P.Q.2d at 1117. In determining whether a particular chemical in the specification is possessed by an applicant, applicants must define the chemical by more than just its biological or intended function. Fiers v. Revel, 25 U.S.P.Q.2d 1601, 1605 (Fed. Cir. 1993).

The claims at issue in Fiers were directed to a DNA consisting essentially of a DNA coding for a human fibroblast interferon-beta polypeptide. Fier's priority document did not teach the nucleotide sequence of the claimed DNA. Rather, the claim was based upon the functional

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limitation that the claimed DNA encoded a human fibroblast interferon-beta polypeptide.[1] The Federal Circuit's analysis of this case revolved around whether or not the DNA was adequately described in the specification. In affirming the Board's conclusion that Fier's priority application did not demonstrate conception of the claimed DNA, the court stated that "irrespective of the complexity or simplicity of the method of isolation employed, conception of a DNA, like conception of any chemical substance, requires a definition of that substance other than by its functional utility." (Id. at 1604). Instead, the Federal Circuit held that "[c]onception of a substance *per se* without reference to a process requires conception of its structure, name, formula, or definitive chemical or physical properties." (Id. at 1605). Thus, applicants must define the substance by more than it biological activity or function. (Id.)

In addition, the Federal Circuit in Fiers relied on its previous decision in Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd., 927 F.2d 1200 (Fed. Cir.), cert. denied sub. nom., 502 U.S. 856, 112 S. Ct. 169, 116 L.Ed.2d 132 (1991), wherein it was stated that:

> Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property . . . because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

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[1] An interference count in *Fier* reads: "A DNA which consists essentially of a DNA which codes for a human fibroblast interferon-beta polypeptide." *Id.* at 1603.

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(Amgen at 1206). In compliance with the standards set forth in Vas-Cath, Fiers, and Amgen, appellants have described the claimed immunological complexes both by the method for their preparation as well as their chemical and physical properties, thereby clearly demonstrating possession of the claimed invention.

Specifically, at page 13, lines 8-18, the specification provides a discussion regarding the identification of the antigens p12 and p18 on a polyacrylamide gel when the amino acids of the HIV-1 virus are labeled radioactively. Extracts of the p12 and p18 are further taught to be within the scope of the claimed invention. (Specification at 14, lines 11-22). These extracts can be purified to isolate the specific antigens by known methods. (Specification at 14, lines 22-26).

In addition, appellants described the characteristics the p12 and p18 antigens that distinguish them from other antigens of HIV-1. For example, page 13, lines 11-15 discusses that p18 has an approximate molecular weight of 18,000 Da, and p12 has an approximate molecular weight of 12,000 Da. When the virus nucleic acids were metabolically labeled with ^{35}S-methionine, the protein bands for these antigens on polyacrylamide gel were visible after silver staining. (Specification at 13, lines 15-18). Thus, one having skill in the art would appreciate that appellants had the p12 or p18 antigens recited in the claims.

The labeled antigens can be used to detect antibodies in the serum of HIV infected patients. It is taught at page 18, lines 11-21, that a purified fraction of HIV-1 or a composition comprising HIV antigens can be labeled by known methods, such as by radioactive, enzymatic, or immunofluorescent labeling, and placed in a kit with a control and reagents to detect an

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immunological complex. Thereafter, the kit can be used to detect antibodies in the serum of an HIV-1 infected patient by binding to the labeled antigen. One having skill in the art would be capable of ascertaining whether or not immunological complexes of the claimed invention were present, and thus whether the patient was infected with HIV.

Using these antigens in immunoassays as described at page 17, lines 5-15 and exemplified at pages 20-30, results in the production of immunological complexes of the claimed invention when HIV antibodies are present. Indeed, the specification teaches that antibodies to p12 and p18 were detected in the sera of AIDS patients. (Specification at 15, lines 23-25).

Furthermore, the immunological complexes can be purified on protein A Sepharose beads, which is known in the art to bind antibodies. (See specification at 21, lines 8-9; Harlow and Lane, page 616 (Exhibit 2)). This method is exemplified in Figure 5 of the specification.

All of these passages in the specification amply demonstrate that appellants not only contemplated, but also possessed, the claimed immunological complexes.

IX. CONCLUSION

Appellants have fully described the claimed invention by showing the means for obtaining the claimed invention. The guidance in the application for the preparation and purification of the claimed immunological complexes clearly conveys to one having ordinary skill in the art that appellants contemplated and possessed the claimed invention at the time the application was filed. Appellants' specification provides as close to the literal support for

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immunological complexes as one skilled in the art would need. Indeed, appellants specifically refer to "immunocomplexes," "immune complexes," and "immunological formation of a complex" in their specification. This is sufficient to satisfy the written description requirement of § 112. Appellants respectfully request that the Examiner's rejection for lack of written description under the first paragraph of § 112 be reversed.

If there are any other fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 06-0916. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

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